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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/692,563	10/24/2003	Michael Draper	PAZ-114CP2	9127
959 7590 05/23/2007 LAHIVE & COCKFIELD, LLP ONE POST OFFICE SQUARE BOSTON, MA 02109-2127			EXAMINER QAZI, SABIHA NAIM	
			ART UNIT 1616	PAPER NUMBER
			MAIL DATE 05/23/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/692,563	Applicant(s) DRAPER ET AL.	
	Examiner Sabiha Qazi	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-5,26-45,48-85 and 87 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-5,26-45,48-85 and 87 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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Final Office Action

Claims 1, 3-5, 26-45, 48-85 and 87 are pending. No claim is allowed at this time.

Amendments are entered.

Summary of this Office Action dated Friday, May 18, 2007

1. Information Disclosure Statement
2. Copending Applications
3. Specification
4. 35 USC § 112 --- Second Paragraph Indefiniteness Rejection
5. 35 USC § 112 --- First Paragraph Written description Rejection
6. 35 USC § 112 --- First Paragraph Scope of Enablement Rejection
7. Response to Remarks
8. Conclusion
9. Communication

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Applicant is requested to tell the relevancy of the cited references in IDS.

Copending Applications

Applicants must bring to the attention of the examiner, or other Office official involved with the examination of a particular application, information within their knowledge as to other copending United States applications, which are "material to patentability" of the application in question. MPEP 2001.06(b). See *Dayco Products Inc. v. Total Containment Inc.*, 66 USPQ2d 1801 (CA FC 2003).

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

35 USC § 112 --- Second Paragraph Indefiniteness Rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-5, 26-45, 48-85 and 87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply:

What is the meaning of “malaria interacting moiety” in claims? A clarification is requested.

35 USC § 112 --- First Paragraph Written Description Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-5, 26-45, 48-85 and 87 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled

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in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Presently claimed invention is drawn tetracycline compounds, composition and their method of use. The compounds include a large number of compounds substituted by various Markush groups. The extent of the hits and results obtained on STN were more than 1500 pages. There is certain limit to search on databases for generic structures. Claimed invention is too broad that detailed and thorough search on databases were not possible. The compounds include a large number of compounds substituted by various Markush groups. The extent of the hits and results obtained on STN were more than 1500 pages. There is certain limit to search on databases for generic structures. Total number of compounds appeared in one search was more than 8000. Applicant is requested to limit the claims to a subgenus of the elected species.

Method of use is drawn to treating or preventing malaria (claim 1) and method of increasing antimalarial activity of an antimalarial compound. (Claim 67).

Example 6 on page 133 is for antibacterial assay. There no examples or guidance showing that Applicant s were in possession of all the methods and compositions at the time of effective filing date.

There is no evidence of possession for all the invention as claimed. What is known is known to one skilled in the art need not to be disclosed in detail. See *Vas-Cath, Inc. v. Mahurkar*, 935 F 2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991).

If technology is less mature, the heavier the burden on the disclosure to demonstrate the possession at the time of effective filing date. In present case claimed

See *In re Curtis*, 69 USPQ2d 1275 (CAFC 2004), the court held there was sufficient evidence to indicate that ordinary artisans could not predict the operability of other species other than the single one disclosed in the specification. See also *Uni. of Rochester v. G. D. Searle* 71 USPA2d 1545 (CAFC 2004).

See written description Guidelines (66 FR 1099 (Jan. 5. 2001): 1242 O.G. 168 (Jan. 30. 2001).

35 USC § 112 --- First Paragraph Scope of Enablement Rejection

Claims 1, 3-5, 26-45, 48-85 and 87 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain compounds and methods, does not reasonably provide enablement for hundred of thousands of compositions containing tetracycline compounds, and their method of treating and or preventing malaria (claim 1) and method of increasing antimalarial activity of an antimalarial compound (claim 67)

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d

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1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The nature of the invention

Presently claimed invention is drawn to compositions containing tetracycline compounds of claim 1 and method of treating or preventing malaria and method of increasing antimalarial activity of an antimalarial compound. (Claim 67).

The predictability or unpredictability of the art

There is a lack of predictability in the art. Example 6 on page 133 is drawn to antibacterial activity assay.

The invention as in claim 1 encompasses a large number of tetracyclines. (claims are broad, see reasons cited above). Antimalarial moiety can be includes any heterocyclic groups, such as pyrrole, furan, thiazole, thiophene, imidazole, pyridine, isoquinoline, purine, indolizine, benzothiaphene, triazole and various others (claim 14). There is no teaching in the disclosure on how to make and use the wide variety of compounds. It is impossible to predict the activity of such a large number of compounds. (more than 8000 so far).

The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. In particular, the court in *In re Marzocchi*, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971), stated:

[I]n the field of chemistry generally, there may be times when the well-known unpredictability of chemical reactions will alone be enough to create a reasonable doubt as to the accuracy of a particular broad statement put forward as enabling support for a claim. This will especially be the case where the statement is, on its face, contrary to generally accepted scientific principles. Most often, additional factors, such as the teachings in pertinent references, will be available to substantiate any doubts that the asserted scope of objective enablement is in fact commensurate with the scope of protection sought and to support any demands based thereon for proof.

The scope of the required enablement varies inversely with the degree of predictability involved, but even in unpredictable arts, a disclosure of every operable species is not required. A single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements. *In re Vickers*, 141 F.2d 522, 526-27, 61 USPQ 122, 127 (CCPA 1944); *In re Cook*, 439 F.2d 730, 734, 169 USPQ 298, 301 (CCPA 1971). However, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a

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single species usually does not provide an adequate basis to support generic claims. *In re Soll*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. See MPEP 2164.03.

The breadth of the claims

The claims are broad. See the reason cited above.

In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result."

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The amount of direction or guidance presented

There is no teaching or guidance to how to use the invention as claimed for treating or preventing malaria and method of increasing antimalarial activity of an antimalarial compound. (Claim 67).

The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. >See, e.g., *Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004) ("Nascent technology, however, must be enabled with a 'specific and useful teaching.' The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee's instruction. Thus, the public's end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology."

The presence or absence of working examples

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A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim will possess the alleged activity. See *In re Riat et al.* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr et al.* (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

The quantity of experimentation necessary

Since there is no guidance and/or direction provided by the Applicants for the wide variety of hundreds of thousands of tetracycline compounds and their preparation and method of use for , one skilled in the art would have to go through undue experimentation to make and/or use the instant invention.

The first paragraph of 35 USC 112 requires “...*such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains...*” The instant invention fails to meet this requirement, as it lacks such full, clear, and concise manner as to enable any person skilled in the art to which it pertains to make and/or use the invention.

Elected species was not found however, the method of use as claimed was not found in the disclosure. Applicant is requested to let us know where is the example to use this compound for the methods as claimed.

Response to Remarks

- Arguments were fully considered but are not found persuasive therefore all the rejections are maintained for the same reasons as set forth in our previous office action.

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- In a personal interview on 5/14/07 Attorney Elizebeth and Cynthia Soroos had discussed the possible amendments to overcome the rejections.
- Claimed invention is too broad that detailed search on databases were not possible. The compounds include a large number of compounds substituted by various Markush groups. The extent of the hits and results obtained on STN were more than 1500 pages. There is certain limit to search on databases for generic structures. Total number of compounds appeared in one search was more than 8000. Applicant is requested to limit the claims to a subgenus of the elected species.

Conclusion

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.


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Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi, Ph.D. whose telephone number is 571-272-0622. The examiner can normally be reached on any business day.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter, Ph.D. can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


SABIHA QAZI, PH.D
PRIMARY EXAMINER